

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 106-115 are pending. Non-elected claims 112-115 were withdrawn from consideration by the Examiner. Upon an indication that the elected invention is patentable, rejoinder of claims 112-115 is requested because the non-elected kit claim requires carrying out the elected method claim.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. They are directed to conforming the scope of the present claims to what the Examiner appears to indicate in the last Office Action would be allowable. Entry of the amendments is requested to address the Examiner's rejections because they should result in allowance (or reduce issues) by mooted those objections.

35 U.S.C. 112 – Definiteness

Claims 96-101 and 106-111 were rejected under Section 112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The frequency of antigen-responsive T cells in (b) of present claim 106 is determined by "contacting different aliquots of said sample separately with antigen compositions comprising either whole ESAT-6, or peptide epitopes derived from ESAT-6, in an ELISPOT assay." Since this assay determines whether each T-cell clone in the aliquot secretes cytokine or not, the collection of results from a plurality of T-cell clones provide a frequency of responsive T cells in the sample.

Correlating the responses of the ELISPOT assay in (c) of present claim 106 is performed by "evaluating the responsive T cells in each separate assay, wherein a positive response using whole ESAT-6 and a negative response using peptide epitopes." Thus, different aliquots of each sample are contacted with at least whole ESAT-6 or peptide epitopes derived from ESAT-6. Each sample gives at least two results: T-cell response against whole ESAT-6 and T-cell response against ESAT-6 peptide epitopes from two separate ELISPOT assays. The individual has recently been exposed to *M. tuberculosis* if the first assay is positive and the second assay is negative for that individual's sample.

As regards “in each separate assay” in claim 106, the Examiner is requested to consider Example 1 (pages 22-24 of Applicants’ specification) where positive scoring with reference to a no added antigen-control is discussed. It would be well understood by those skilled in detection of activated T cells by ELISPOT assay that the frequency of positive “spots” needs to be determined for at least a whole ESAT-6 sample, a peptide-containing sample, and a control. Positive controls give high frequencies of responsive T cells; negative controls give low frequencies of responsive T cells. A comparison of test (e.g., whole ESAT-6 or peptide derived therefrom) and control frequencies provides a determination of positive or negative response. A finding of positive response relative to control for the whole ESAT-6 sample, but a negative response relative to control of the ESAT-6 peptide sample is indicative of recent exposure to *M. tuberculosis*.

Claim 109 presently depends from claim 107. This amendment clarifies that “all possible peptide epitopes” are 8 to 29 amino acids in length. Therefore, there is a finite (and reasonable) number of different peptide epitopes that can be produced to cover the ESAT-6 protein by scanning across its sequence with a “window” of that length.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971).

Claims 96-101 and 106-111 were rejected under Section 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants traverse because amendment of independent claim 106 clarifies that (c) evaluating whether there is **both** a positive response to whole ESAT-6 **and** a negative response to ESAT-6 peptides is required. Further, cancellation of claims 96-101 removes the recitation of “analogs” from the claimed invention.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 112 – Written Description

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Claims 96-101 were rejected under Section 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse because cancellation of claims 96-101 moots this rejection.

Withdrawal of the written description rejection made under Section 112, first paragraph, is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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